

concentration of less than or equal to about 1.5 micromolar,” as recited by Applicant’s claim 1 (from which all of Applicant’s claims directly or indirectly depend). Indeed, none of the cited references present evidence showing the inhibition of proliferation of *any* type of cells in culture. Furthermore, none of the cited references disclose experiments utilizing RNA oligonucleotides to inhibit Kaposi’s sarcoma cells, in culture or *in vivo*.

“In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.” *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original); see also MPEP 2112. No such basis in fact and/or technical reasoning has been provided by the Examiner to support the Examiner’s implicit argument that any oligonucleotide capable of inhibiting the expression of VEGF has the ability to inhibit the proliferation of cultured Kaposi’s sarcoma cells. The remark by the Examiner that “*inhibitory concentrations vary* based on modifications to antisense oligonucleotides” undercuts the Examiner’s inherency argument. The Examiner’s remark suggests that the recited feature of inhibiting cultured Kaposi’s sarcoma cells with an IC<sub>50</sub> concentration of 1.5 micromolar does *not* necessarily flow from the sequences disclosed by the cited patents, none of which are identical to the sequences disclosed by Applicant.

For the forgoing reasons, Applicant respectfully submits that the pending claims are not anticipated by any of the cited references, explicitly or inherently. Applicant respectfully requests withdrawal of the Examiner’s rejection under 35 U.S.C. 102(e).

## II. Rejections Under 35 U.S.C. 103

### A. Claims 1-3, 7-15 over Robinson (5,814,620; 5,710,136 and 5,801,156) and Uchida (6,150,092).

The Examiner rejected claims 1-3 and 7-15 as allegedly unpatentable over the Robinson patents (above) in view of the Uchida patent (above). Specifically, the Examiner argues that

one skilled in the art would clearly have had motivation to make the instantly claimed antisense molecules since it is absolutely clear that the region targeted has been clearly shown by the prior art to be a desired

target for antisense inhibition. . . . One would expect that the inhibition conditions recited in the claims would be met since these values were observed upon making antisense to the specific region clearly taught in the prior art.

See Office Action at 5.

The Examiner has not set forth a *prima facie* case of obviousness because, as discussed in Section I, above, the Examiner has failed to show in the cited art *all of the elements* recited in Applicant's claim 1. There is no teaching or suggestion in the art that a select population of antisense oligonucleotides would have the ability to inhibit the proliferation of Kaposi's sarcoma cells at the recited concentration. The only observations of oligonucleotides capable of inhibiting the proliferation of Kaposi's sarcoma cells (i.e., those with an IC<sub>50</sub> concentration of 1.5 micromolar or less) are described in Applicant's specification. Obviousness cannot be based on the applicant's own disclosure. See In re Vaeck, 947 F.2d 488; see also MPEP 2142.

Applicant's arguments with respect to claim 1 apply to all of Applicant's claims, because all of Applicant's claims depend directly or indirectly from claim 1. Applicant therefore respectfully requests withdrawal of the Examiner's rejection of claims 1-3 and 7-15 under 35 U.S.C. 103(a).

#### **B. Claims 4-6; Robinson, Uchida, Barleon and Chan**

The Examiner rejected claims 4-6 as allegedly unpatentable over the Robinson patents, in view of Uchida, and further in view of Barleon et al. and Chan et al. Barleon et al. is cited for teaching the use of an antiserum against VEGF and for observations relating to the role of flt-1 in the VEGF pathway. Chan et al is cited as teaching the roles of VEGF and its receptors "in various diseases." See Office Action at 6.

Claims 4-6 both depend indirectly on claim 1. Both Barleon et al. and Chan et al. fail to correct the deficiencies of the primary references (see above). For this reason, and the reasons provided in Section II.A., above, Applicant respectfully submits that the Examiner has not made a *prima facie* case of obviousness with respect to claims 4-6. Applicant respectfully requests withdrawal of the Examiner's rejection of claims 4-6 under 35 U.S.C. 103(a).

## CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is respectfully requested to telephone Applicants' representative at (415) 393-2778.

## NOTICE OF FIRM NAME CHANGE

Agent for Applicant wishes to inform the Office that the name of its firm has been changed to Bingham McCutchen LLP.

DATE: November 18, 2002

Respectfully submitted,

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